Rectal Cancer: MR Imaging before Neoadjuvant Chemotherapy and Radiation Therapy for Prediction of Tumor-Free Circumferential Resection Margins and Long-term Survival

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**Purpose:** To retrospectively evaluate the prognostic importance of involvement of the circumferential resection margin predicted by using magnetic resonance (MR) imaging before neoadjuvant treatment in patients with rectal cancer.

**Materials and Methods:** The local institutional review board approved the retrospective analysis of the data and waived informed consent. Sixty-eight patients (52 men, 16 women; mean age ± standard deviation, 58.9 years ± 9.4) with cT3 NX M0 tumors were included. T2-weighted MR images were analyzed in consensus by two radiologists with respect to the shortest distance between the outermost parts of the tumor to the adjacent mesorectal fascia (as the potential circumferential resection margin in total mesorectal excision). Histopathologic and follow-up data were available for all patients (mean follow-up time, 54 months; range, 31–77 months). To compare local recurrence and survival rates, the population was divided into three groups categorized according to the minimum distance of the tumor to the mesorectal fascia (group 1, ≤1 mm; group 2, >1 to 5 mm; group 3, >5 mm). Univariate Cox and multivariate proportional hazard regression models were used to test the prognostic importance of clinical, histopathologic regression, and histopathologic tumor parameters.

**Results:** MR imaging led to accurate prediction of a histologically involved circumferential resection margin (sensitivity, 100%; specificity, 88%). The rates for local recurrence (group 1, 33%; group 2, 5%; group 3, 6%; \(P < .02\)) and 5-year overall survival (group 1, 39%; group 2, 70%; group 3, 90%; \(P < .001\)) differed significantly among the predefined groups. The distance to the mesorectal fascia was an independent prognostic parameter in multivariate analysis (\(P < .001\)), and histopathologic response to treatment provided no additional information.

**Conclusion:** Prediction of the tumor-free circumferential resection margin assessed with MR imaging before initiation of neoadjuvant chemotherapy and radiation therapy proved to be a prognostic factor in rectal cancer.

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The prognosis of rectal cancer is influenced by several factors, such as local tumor extent, involved lymph nodes, and the presence of distant metastases (1–5). Among these, the presence and extent of extramural tumor spread influence both long-term survival and the risk of local recurrence (5–7). With the more widespread acceptance of neoadjuvant concepts, there is an increasing need for preoperative imaging methods to aid in the selection of patients who could benefit by more aggressive multimodality treatment approaches on the basis of individual risk factors (8,9). According to recently published data, patients who received neoadjuvant chemotheraphy and radiation therapy had a substantially lower rate of local recurrence compared with patients who received postoperative chemotherapy and radiation therapy (10). Magnetic resonance (MR) imaging has been shown to be a promising tool in preoperative local staging and may also provide measurements of the distance to the mesorectal fascia as the potential circumferential resection margin in total mesorectal excision (11). It appears that histopathologic tumor involvement of the circumferential resection margin is an independent predictor of local recurrence and distant metastases and may therefore influence overall survival after primary resection of rectal cancer (6,12). Marijnen et al (13) and Luna-Perez et al (14) showed that, even after preoperative radiation therapy, patients in whom the circumferential resection margin was histopathologically involved had a substantially worse prognosis than did patients with tumor-free circumferential resection margins.

The classic approach of defining the T stage (TNM classification) of the tumor on the basis of MR imaging or endoscopic ultrasonography (US) findings may lead to staging failures in the differentiation of T2 and borderline T3 tumors (11). Some investigators have proposed that the measurement of tumor extent relative to the circumferential resection margin and the prediction of tumor-free resection margins on the basis of MR imaging may be feasible and more robust than defining the T stage (15,16). However, little is known about the relevance of such preoperative MR imaging measurements for long-term survival (17). Moreover, no data are available about the prognostic effect of the prediction of the circumferential resection margin before neoadjuvant chemotherapy and radiation therapy. The aim of our study was, therefore, to retrospectively evaluate the prognostic importance of involvement of the circumferential resection margin predicted with use of MR imaging before neoadjuvant treatment in patients with rectal cancer.

Materials and Methods

Patients

Patients gave their informed consent for MR imaging, which was performed during routine work-up for patients with rectal cancer. The local institutional review board approved the retrospective analysis of the data and waived informed consent for that analysis.

Sixty-eight consecutive patients with biopsy-proved rectal cancer (16 women, 52 men; mean age ± standard deviation, 58.9 years ± 9.4) were examined between 1998 and 2001 with MR imaging before neoadjuvant therapy and total mesorectal excision. Patients who had tumors with an advanced clinical stage (cT3 NX M0) and had no evidence of distant metastases were eligible for inclusion in this study. In the staging of tumors, procedures that included endoscopic US and MR imaging of the pelvis were performed for assessment of local tumor extent, and computed tomography (CT) of the chest and abdomen and abdominal US were performed to help exclude distant metastases. All patients were classified as having a cT3 lesion according to endoscopic US. Sixty-six patients had tumors that were concordantly classified as stage T3 lesions by using MR imaging according to criteria described elsewhere (11,18). In two (3%) patients, a T4 lesion was suspected on the basis of MR imaging findings. The distance from the anal verge was determined with endoscopy.

Neoadjuvant Treatment and Surgery

The neoadjuvant treatment protocol included external-beam radiation therapy delivered with a linear accelerator by using 10–15-MeV photons. A 45-Gy radiation dose was applied to the pelvis in 1.8-Gy fractions. Patients were treated in the prone position with three individually shaped portals (right lateral, left lateral, and dorsal). Concurrently, chemotherapy with fluorouracil was administered by using continuous intravenous infusion at a daily dose of 230 mg/m². Surgery was performed 5–6 weeks after completion of chemotherapy and radiation therapy. All patients underwent total mesorectal excision according to standardized techniques by means of low anterior resection or abdominopereineal excision (Table 1).

MR Imaging

MR imaging was performed with patients in the supine position by using a 1.5-T MR imager (Gyroscan NT; Philips Medical Systems, Amsterdam, the Netherlands) equipped with a phased-array coil. The MR imaging protocol included nonenhanced and contrast material–enhanced imaging with a dose of 0.2 mL per kilogram body weight of a gadolin-
ium-based contrast agent (Magnevist; Schering, Berlin, Germany). Two-dimensional T1-weighted spin-echo and T2-weighted fast spin-echo sequences (Table 2) were performed. All sequences were performed in the transverse and sagittal planes. The transverse planes were angled by a physician exactly along the long axis of the tumor by using the sagittal planes. The total image time was approximately 30 minutes. Patients received a small amount (approximately 50–100 mL per rectum) of US gel (UltraSchallgel; TMP Tüshaus Medical Produkte, Velen, Germany) and an intravenous spasmolytic medication (buthylscopolamide [BS-ratiopharm Injektionslösung; Ratiopharm, Ulm, Germany] or glucagon [GlucaGen Hypokit; Novo Nordisk Pharma, Mainz, Germany]).

Distance to the Mesorectal Fascia

The images were assessed retrospectively by two radiologists (H.A.W. and J.C.S., with 4 and 7 years of experience in gastrointestinal MR imaging, respectively) in consensus during four sessions. The radiologists knew that all patients had received neoadjuvant treatment for rectal cancer and that they therefore should have a cT3 tumor on the basis of transrectal US. For the prediction of potential involvement of the resection margin, MR imaging–based measurements of the closest distance (in millimeters) between the maximum depth of tumor penetration through the bowel wall and the circumferential resection margin were measured on T2-weighted MR images by using a workstation (EasyVision; Philips Medical Systems). Only the solid portion of the tumor, and no spicules, was considered for the measurements because spicules may be nonspecific and can represent

Figures 1–3

Figure 1: Transverse T2-weighted MR image (2500/120) of the middle of the pelvis. The mesorectal fascia (white arrows) is clearly visualized. The tumor (black arrows) assigned to group 1 in the anterior aspects of the rectum has large extramural infiltrations involving the mesorectal fascia. A tumor node (arrowhead) is visualized in the left anterior aspect of the mesorectal compartment (distance, 3 mm).

Figure 2: Transverse T2-weighted MR image (2500/120) of the middle of the pelvis. The tumor (double-headed arrow) in the right lateral anterior aspect of the rectum shows extramural extension, with a minimum distance to the mesorectal fascia (white arrows) of 5 mm. This tumor was classified in group 2.

Figure 3: Transverse T2-weighted MR image (2500/120) of the middle of the pelvis. The tumor (double-headed arrow) in the left lateral anterior aspect of the rectum shows only minor extramural extension, with a minimum distance to the mesorectal fascia (white arrows) of 12 mm. The tumor was assigned to group 3.
fibrosis, tumor deposition, or both (15). T2-weighted and contrast-enhanced T1-weighted images were used in conjunction for assessment of T stage (66 T3 lesions and two T4 lesions). When extraluminal tumor nodes were closer to the circumferential resection margin than to the main tumor itself, they instead of the primary tumor were considered for the prediction of the tumor-free circumferential resection margin in six of 68 patients (15). Patients were categorized into one of three groups according to the minimum distance between the tumor and the mesorectal fascia (15). When the tumor reached the mesorectal fascia, a distance of 1 mm or less was recorded (group 1, potentially involved margin) (Fig 1). Group 2 consisted of patients with a measured distance of greater than 1 to 5 mm (intermediate margin) (Fig 2). Patients with a distance greater than 5 mm were included in group 3 (wide margin) (Fig 3).

**Histopathologic Evaluation**

After surgery, the specimens were fixed in formalin for 24 hours. The sections were examined by one pathologist (K.B., with 15 years of experience in gastrointestinal pathology). The pathologic T stage for each tumor was recorded according to the TNM classification (19). Any specimen that showed tumor tissue (primary tumor or tumor nodes) with a 1-mm or less distance to the circumferential resection margin was recorded as having a positive margin.

**Response to Neoadjuvant Treatment**

Histopathologic remission was classified into one of four categories: category 1a, no residual tumor (0%, complete remission); category 1b, 1%–9% residual tumor (subtotal response); category 2, 10%–50% residual tumor (partial response); category 3, greater than 50% residual tumor (minimal or no response) (20). The categories were summarized in two groups for further analysis; group A consisted of responders (ie, those in categories 1a and 1b); group B consisted of nonresponders (ie, those in categories 2 and 3).

**Outcome**

All patients were followed up in 3-month intervals for 1 year, in 6-month intervals for 2 years, and in 12-month intervals thereafter. Procedures included US and CT of the abdomen and pelvis, endoscopy, and chest radiography. The median follow-up time was 54 months (range, 31–77 months). In patients with complete resections (66 of 68), designated as R0, time to recurrence was calculated as the time from initiation of neoadjuvant therapy to detection of local recurrence or distant relapse. Local recurrence was proved with biopsy in all patients. In patients with residual tumor after resection (two of 68), or R1, time to local tumor progression or distant metastases was determined. All other recurrences were defined as distant. A diagnosis of local recurrence or distant metastasis before or at the time of death led us to assume that the death was cancer related, irrespective of the actual cause of death.

**Statistical Analysis**

All quantitative data were expressed as the mean ± standard deviation. Overall recurrence-free rates and overall survival rates were calculated according to the Kaplan-Meier method by using software (StatView, version 5.0; SAS Institute, Cary, NC). The differences among groups 1–3 of patients were analyzed by using a χ² test (MedCalc, version 8.1.1; MedCalc Software, Mariakerke, Belgium). A univariate Cox regression model (SPSS; SPSS, Chicago, Ill) was used to test the correlation between overall survival and the distance to the circumferential resection margin, as well as the distance from the anal verge, the T stage (TNM classification) according to results of histopathologic examination, and tumor response to neoadjuvant treatment. The independence of these factors was tested by using a multivariate proportional hazard regression model (SPSS; SPSS). The P values of the two most significant variables are given in the Results section. All statistical tests were performed at the 5% level of significance.

The sample size of n = 68 in our study was based on a statistical power calculation performed by using a statis-
tional program (PS, version 2.1.30; William D. Dupont and Walton D. Plummer, Jr, Vanderbilt University School of Medicine, Department of Biostatistics, Nashville, Tenn), which can be accessed at http://biostat.mc.vanderbilt.edu. Assumptions were made with respect to a median survival time of 3.5 years in the patients in whom the mesorectal fascia was involved (20% of all patients) and that of 6 years in the patients without such involvement (80% of the patients). The recruitment period was 2 years, and the follow-up period was 4 years. These assumptions were based on data in previous studies (17) and are widely consistent with the actual parameters found after retrospective analysis of our data. The sample size required for detection of differences with a power of 80% would be 65 patients.

Results

Distance to the Mesorectal Fascia at MR Imaging

The mean distance between the tumor and the circumferential resection margin measured with MR imaging before neoadjuvant treatment was 8.5 mm ± 8.0 (range, 0–30 mm). In 68 patients, the distance between the tumor and the mesorectal fascia was 1 mm or less (group 1) in 12 (18%) patients, greater than 1 to 5 mm (group 2) in 22 (32%) patients, greater than 5 mm (group 3) in 34 (50%) patients.

Response Evaluation and Histopathologic Work-up

Four (6%) of 68 patients showed a positive circumferential resection margin according to histopathologic examination results after total mesorectal excision. All these patients developed local recurrence and died during follow-up; in all cases, MR imaging findings helped in the correct prediction of outcomes (Table 3). The overall sensitivity and specificity of MR imaging for prediction of a tumor-involved margin that was based on histopathologic examination results were 100% (four of four) and 88% (56 of 64), respectively. Eight of 12 patients with a distance of 1 mm or less on the basis of MR imaging findings had a negative (tumor-free) resection margin at histopathologic examination after neoadjuvant treatment; four of eight patients with a negative (tumor-free) resection margin responded to neoadjuvant treatment (Table 3). At final histologic staging, ypT4 tumors were observed in three (4%) patients, ypT3 tumors were observed in 19 (28%) patients, ypT2 tumors were observed in 19 (28%) patients, ypT1 tumors were observed in four (6%) patients, and ypT0 tumors were observed in nine (13%) patients. At histopathologic examination, tumors in 51 (75%) patients were classified as N0 lesions, those in nine (13%) patients were classified as N1 lesions, and those in eight (12%) patients were classified as N2 lesions.

At histopathologic examination, the sterilization rate (category 1a = T0) was 13% (nine of 68 patients). In 21 (31%) of 68 patients, less than 10% residual tumor was detected at the site of the primary tumor. A partial response was found in 26 (38%) patients, whereas in 12 (18%) patients a minimal response or no response was observed. Thus, the group of histopathologic responders consisted of 30 (44%) patients, and the group of nonresponders consisted of 38 (56%) patients.

Outcome

The local recurrence rate in patients with R0 resections was 7% (five of 68); one of the patients also developed distant metastasis. Two (3%) of 68 patients who were in group 1 underwent R1 resections and developed local disease progression. The latter patients also were referred to as having local recurrence for further analysis. Distant recurrence was observed in 18% (12 of 68) of the patients (liver lesion in eight patients, lung lesions in three patients, and brain lesions in one patient). Nineteen percent (13 of 68) of the patients died during the observation period. Three of seven patients died in association with local recurrence (two in group 1, one in group 2, and none in group 3). Ten of 12 patients died of distant recurrence (four in group 1, four in group 2, and two in group 3). The overall survival rate at 5 years was 74%, and the overall 5-year recurrence-free survival rate was 71%.

Correlation of MR Imaging Findings, Histopathologic Findings, and Patient Survival

Significantly more patients in group 1 (33%) developed local recurrence compared with those in group 2 (5%) and group 3 (6%) (P < .02) (Table 3). The

Table 3

| Outcome and Histopathologic Data in Relation to MR Imaging–based Measurements of Distance between Tumor and Mesorectal Fascia before Neoadjuvant Treatment in 68 Patients |
|---------------------------------|-----------------|-----------------|-----------------|
| Outcome Data                    | Group 1 (n = 12) | Group 2 (n = 22) | Group 3 (n = 34) |
| Histopathologic finding         |                 |                 |                 |
| No. with positive CRM margin    | 4 (33)          | 0 (0)           | 0 (0)           |
| No. with negative CRM margin    | 8 (67)          | 22 (100)        | 34 (100)        |
| Neoadjuvant treatment           |                 |                 |                 |
| No. of responders               | 4 (33)          | 10 (45)         | 16 (47)         |
| No. of nonresponders            | 8 (67)          | 12 (55)         | 18 (53)         |

Note.—Group 1 included measurements of the distance between the tumor and the mesorectal fascia of 1 mm or less, group 2 included measurements of more than 1 to 5 mm, and group 3 included measurements of more than 5 mm. Numbers in parentheses are percentages. The χ² and Pvalues, respectively, were as follows: 19.80 and <.001 for comparison between number with positive and with negative CRM margins, 8.40 and <.02 for number with local recurrence, 1.24 and .54 for number with distant relapse, and 0.70 and .1 for comparison between number of responders and of nonresponders. For 5-year recurrence-free and overall survival rates, the Pvalues were <.05 and <.001, respectively. CRM = circumferential resection margin.
The recurrence-free survival rate was significantly different among the three groups (Fig 4). The recurrence-free survival rate at 5 years was 42% in group 1, 69% in group 2, and 81% in group 3 ($P < .05$). The overall survival rate was also significantly different among the three groups (Fig 5). The overall survival rate at 5 years was 39% in group 1, 70% in group 2, and 90% in group 3 ($P < .001$). There was no significant difference among the groups with respect to distant relapse ($P = .44$), T stage (TNM classification) ($P = .44$), or response to neoadjuvant treatment according to histopathologic examination ($P = .1$). The distance from the tumor to the circumferential resection margin was highly correlated with overall survival as determined by using a univariate analysis ($P < .001$).

The 5-year survival rates were 80% in patients with no residual tumor or tumors that were confined to the rectal wall (T0–T2) and 66% in patients with tumors that exceeded the rectal wall (T3 or T4). The final ypT stage—that is, the presence of mesorectal tumor spread of stage T3 or higher—was also a strong predictor of overall survival, as established by using univariate analysis ($P < .02$). However, the level of significance was lower than that seen with the distance between the tumor and the mesorectal fascia. Histopathologic response was also significantly correlated with overall 5-year survival rate (83% in group A and 65% in group B) ($P < .05$).

**Multivariate Analysis**

The distance from the tumor to the circumferential resection margin was the most important prognostic factor among the parameters tested in the multivariate proportional hazard and Cox regression models ($P < .001$). Tumor response to treatment provided no significant additional information ($P = .25$). The prognostic significance of the distance from the tumor to the circumferential resection margin was present even after consideration of ypT stage and distance from the anal verge.

**Discussion**

Two editorials have stressed the importance of differentiated treatment in patients with rectal cancer and the need for a tool for selection of patients on the basis of more accurate risk stratification (21,22). Recommendations for adjuvant treatment of colorectal cancer have traditionally been based on histologic information that is not available until after surgery. However, for rectal cancer, neoadjuvant (preoperative) treatment has turned out to be more effective and less toxic than adjuvant treatment (23). To our knowledge, no reliable information on the risk of recurrence is available preoperatively, and the role of MR imaging for initial work-up of patients with rectal cancer has not been fully accepted. Preoperative MR imaging may, with reasonable accuracy, indicate the extent of tumor growth relative to layers of the rectal wall (T stage [TNM classification]) and the anal canal (11). The value of imaging for prediction of nodal status is generally limited without criteria that add information to the measurement of the size of a lesion.

The prognostic importance of the tumor-involved circumferential resection margin at histopathologic examination has been convincingly demon-
strated in several studies (6,12,24–26). The identification of the mesorectal fascia as the potential circumferential resection margin in total mesorectal excision according to images was first reported in 1983 (27). However, since that time, the issue of imaging the mesorectal fascia never gained much interest until the past years (15,16,28–30). Our study showed that patients with a tumor-involved margin in whom prediction was determined with use of MR imaging findings before neoadjuvant treatment had a substantially worse prognosis than did patients without such involvement. This difference was mainly attributable to an increased risk of local recurrence. All patients with wide or intermediate margins in whom prediction was determined with MR imaging had a negative circumferential resection margin at histopathologic examination after neoadjuvant treatment and surgical resection. The overall 5-year survival rate in our study was almost identical to that recently reported by Sauer et al (10), with use of a cumulative external radiation dose of 50 Gy. The number of complete remissions and the rate of local recurrence observed in our study were in the same range as data previously published for neoadjuvant treatment regimens (10,31–34). These findings indicate that the patients investigated in our study are a typical and representative cohort with locally advanced rectal cancer.

A substantial number of patients (eight of 12) in whom margins with potential tumor involvement were predicted with MR imaging findings had a negative circumferential resection margin at histopathologic examination after treatment. However, the sensitivity and specificity for prediction of a tumor-involved margin, considering all patients, were high (100% and 88%, respectively). Because direct comparison of MR imaging before therapy and histopathologic examination after neoadjuvant treatment were not possible, it is unclear whether the relatively small number of patients with a tumor-involved circumferential resection margin in group 1 is truly a treatment effect or a false-positive MR imaging finding. Half of the patients with false-positive MR imaging findings, however, responded to neoadjuvant treatment according to histopathologic examination results. Investigators (15,16) have described reactive fibrosis as a potential cause of overestimation of the extent of the tumor on the basis of MR imaging findings in relation to the rectal wall layers, as well as in relation to the circumferential resection margin.

The number of published studies in which the focus was on the circumferential resection margin that was predicted with use of MR imaging findings is smaller than the number of reports about tumor staging. To our knowledge, the only study with follow-up data was published by Martling et al (17) in 2003. These authors reported excellent correlation of MR imaging–based prediction of circumferential resection margin status with local recurrence and long-term survival in 105 patients. However, only 74 of these patients received preoperative short-term radiation therapy, which usually does not lead to shrinkage of the tumor; in addition, none of the patients received conventionally fractionated radiation therapy with concurrent chemotherapy. In concordance with results we reported, Martling et al reported a relatively large number of patients in whom an involved margin was predicted but was found to be negative at histopathologic examination (specificity, 0.72). In contrast to results in our study, in their study, some involved margins were missed at MR imaging (sensitivity, 0.80). This difference may have contributed to the somewhat unexpected finding of an almost equal rate of local recurrences in the group with and the group without a positive circumferential resection margin that was predicted with MR imaging findings in their study (17). Beets-Tan et al (35) reported a decrease in incomplete resections because of the consideration of preoperative MR images, but no data about long-term survival were included.

The number of patients with circumferential resection margin involvement, the response to neoadjuvant treatment, and the distribution of pathologic T stages (TNM classification) were similar to those reported in other studies (10,36,37). Both pathologic T stage and response to treatment assessed with histopathologic examination were predictors of local recurrence and long-term survival. However, multivariate analysis results indicated that the distance to mesorectal fascia before neoadjuvant treatment with preselection of cT3 lesions was an independent factor compared with histopathologic regression parameters.

How can MR imaging–based prediction of the circumferential resection margin status affect the treatment of patients with rectal cancer? In Europe, there is a growing tendency to offer short-course or even long-course preoperative (neoadjuvant) radiation therapy to patients with mobile (resectable) rectal cancer. Although the morbidity and mortality rates associated with neoadjuvant therapy are low, some patients with a low likelihood of local recurrence may be overtreated with this approach. In the United States, the standard for locally advanced tumors (T3 or N1) is postoperative (adjuvant) chemotherapy and radiation therapy; the advantage of this approach is accurate selection of patients at risk for local recurrence according to histopathologic examination results. The disadvantage is that postoperative chemotherapy and radiation therapy are more toxic, and probably a little less effective, than neoadjuvant treatment. Combination preoperative chemotherapy and radiation therapy is an established treatment for fixed tumors because it helps improve resectability through tumor shrinkage. However, there is growing interest in neoadjuvant treatment for selected patients with mobile rectal cancer in whom MR imaging may help in the selection of patients who are likely to benefit from preoperative therapy (group 1, and maybe group 2) on the basis of a risk factor (distance to the circumferential resection margin) that can be established before surgery.

Some limitations to our study need to be considered. The data were retrospectively analyzed, and there are a limited number of patients for whom complete follow-up data were available. However, because the survival of patients with rectal cancer improved dur-
ing the past few decades, a long period is required to generate reliable follow-up data; during this time, a homogeneous diagnostic work-up and therapeutic regimen must be maintained. Another limitation is that direct correlation between MR images before treatment and histopathologic findings after neoadjuvant therapy is not possible. However, excellent correlation between MR imaging–based measurements and histopathologic findings with respect to the distance from the tumor to the mesorectal fascia and prediction of tumor-free circumferential margins has been reported previously (15). Moreover, all patients in our study with a tumor-involved circumferential resection margin were correctly identified with use of MR imaging before therapy.

Prediction of involvement of the circumferential resection margin assessed with MR imaging before initiation of neoadjuvant chemotherapy and radiation therapy proved to be a prognostic factor in rectal cancer. MR imaging can be used to complement staging in locally advanced disease to help stratify patients according to the shortest distance of the tumor to the mesorectal fascia.

References